science & technology

A Vision for the Future

by David Trieu

Microfabrication for the development of retinal implants

One day you start noticing that your vision is deteriorating. Maybe you are having trouble reading or it just happens that you failed the vision test on your driver's license exam. You decide to go see the ophthalmologist or optician, hoping that a new pair of glasses will fix everything but the doctor's grimace indicates a problem more serious than just poor vision: you have been diagnosed with macular degeneration.

What is macular degeneration?

Each year, more than 400,000 Americans are diagnosed with age-related macular degeneration (AMD), a progressive eye disease common among older people that can lead to total blindness. However, the good news is that having macular degeneration does not mean that you are completely blind, though it does cause loss of the sharp, central vision needed for many daily tasks that involve looking straight at objects. People with AMD may find it difficult or impossible to drive, read, sew, or recognize faces. Many also have trouble distinguishing between colors.

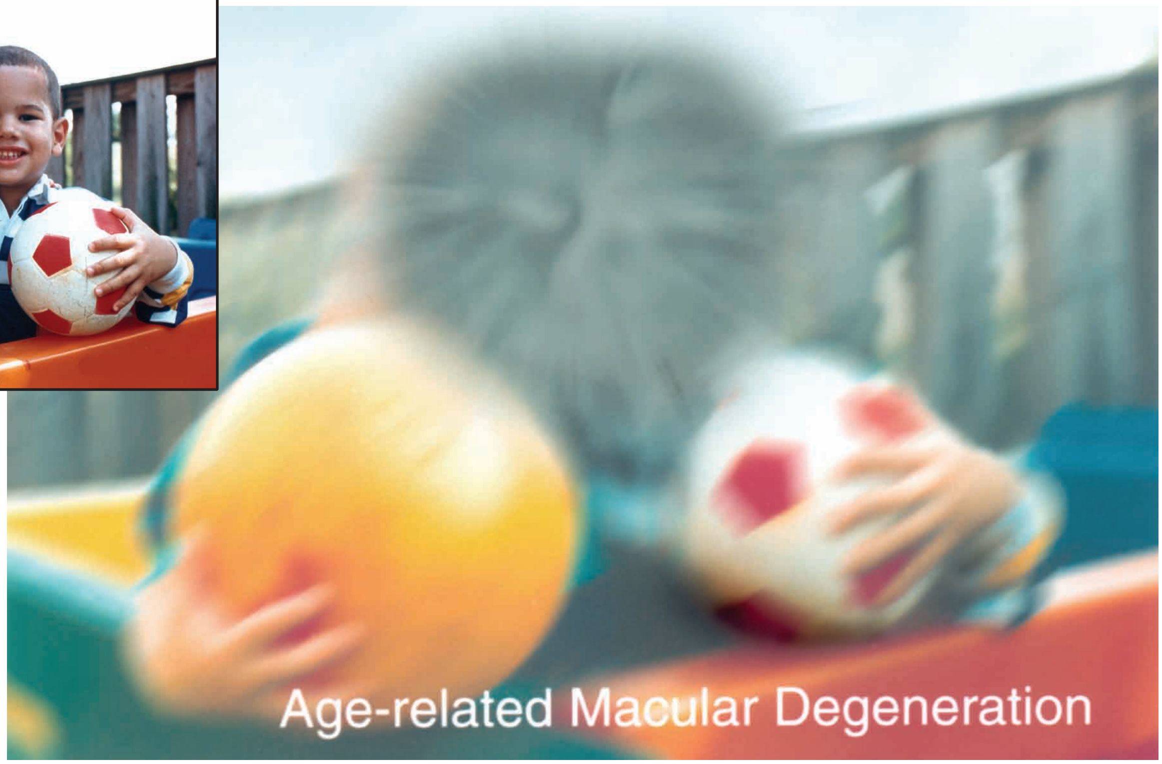
Age-related macular degeneration (AMD) results from an abnormality in a small part of the retina known as the macula. We see objects because light passes through the eye and strikes the retina. Light-sensitive cells in the retina capture images from the outside world and relay them to the brain. The macula, which is about the size of a pencil eraser, relays images in the direct line of focus. People lose this central vision when macular cells degenerate and stop working normally. This deterioration occurs slowly over time, so while blindness might not develop immediately, severe and irreversible vision loss is likely to set in over a long period of time.

Is there a cure?

AMD causes the deterioration of the central portion of the retina and as of now, there is no cure for the disease. Some treatments to slow down the effects of macular degeneration include vitamin supplements, microcurrent stimulation, and forms of laser-eye surgery. However, for the most part, the effects of these solutions have only been temporary and inadequate in curing the disease.

Currently, an interdisciplinary team here at Stanford University is working to reverse the effects of age-related macular degeneration. Leading the project is Stacey Bent of the Chemical Engineering Dept. and ophthalmologist Harvey Fishman of the School of Medicine. A collaboration between the departments of chemical engineering, ophthalmology, and electrical engineering, the project combines techniques in surface modification, materi-

^ **Top:** Eye candy. **Bottom:** Stacey Bent and Harvey Fishman demonstrate a prototype of a chip that someday may help restore sight in people suffering from age-related macular degeneration. (Courtesy of Stacey Bent)



Macular degeneration > causes an empty area in the center of vision, as well as dimming of colors. Picture source: http://www.nei.nih.gov/photo/sims/index.asp.

als fabrication, and retinal cell biology to develop therapeutics designed to prevent this loss of vision. The project focuses on two new ways of reversing the vision loss: a functional retinal implant based on tissue engineering and a retinal prosthesis.

Retinal implants through tissue transplant

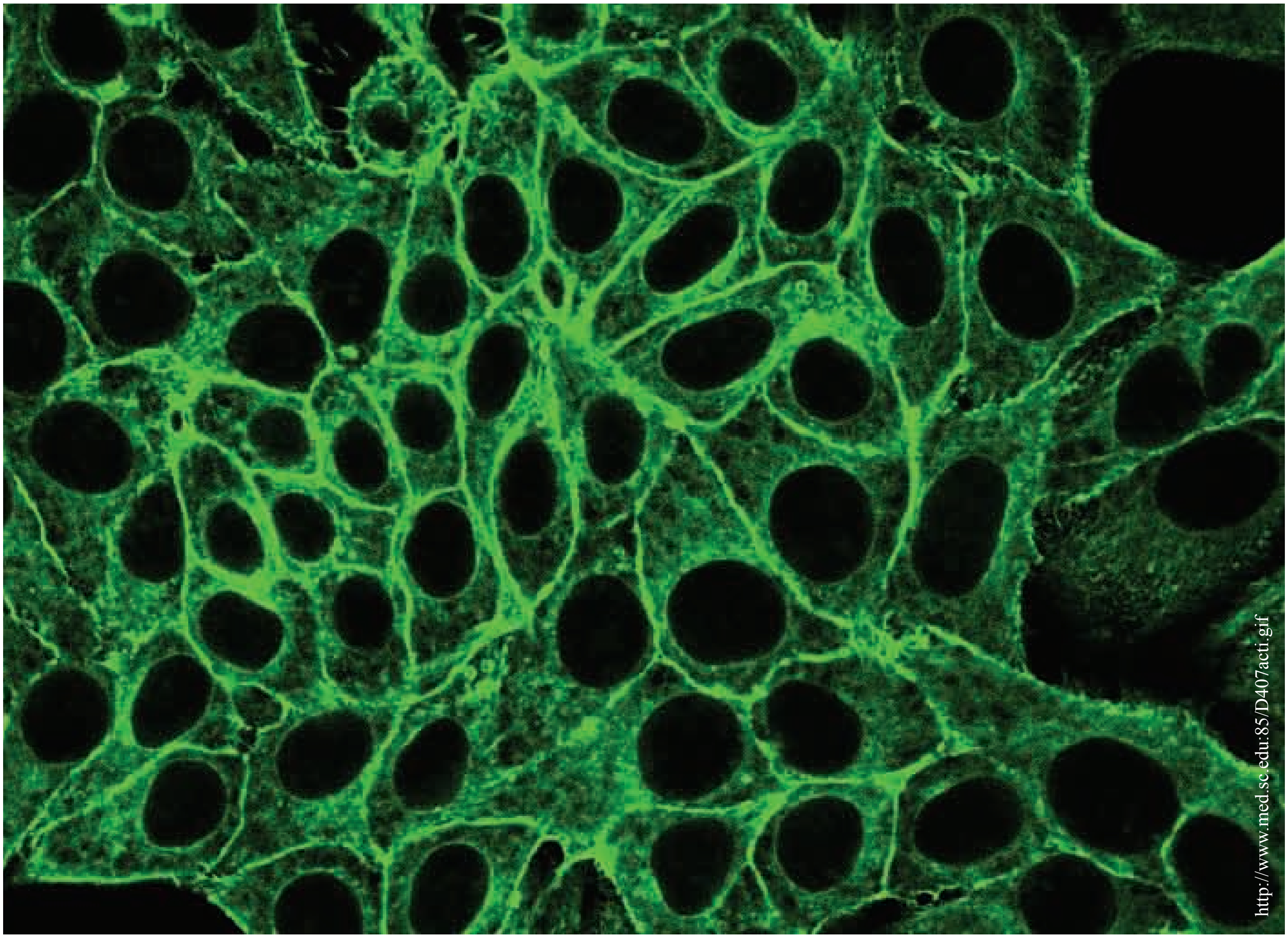
In about 80 percent of the patients diagnosed with age-related macular degeneration, some of the underlying cells remain alive even though the cover layer of cells has degraded. The Bent Research Group is working on recreating the protective cell layer, made up of specific macular cells known as retinal pigment epithelial (RPE) cells. In order to recreate this tissue, the team is transplanting tissues from other parts of the eye. The tissue that normally covers the eye lens is used as a support membrane to grow healthy cells taken from the iris. The cells from the iris have the capability of growing into various cells and induced to become RPE cells. The newly created layer would then be transplanted into the retina. Since only the patient's own tissues and cells are used, the likelihood of transplant rejection is minimal.

The major obstacle that the team has encountered with this approach is getting the transplanted layer to behave like the natural layer of the eye. However, over the course of the past year, Bent's group has made valiant strides in their research. "Our biggest progress has been in two areas: learning more about the fabrication of the device and the polymers involved," says Bent. The group discovered that the RPE cells must be densely packed onto the membrane to perform the necessary feeding and waste-removal functions. To do this, the team is currently investigating the use of microcontact printing (mCP) with soft polymers. Essentially, how the iris cells cluster on the surface of the lens capsule tissue employs some of the same techniques used to make patterns on a computer chip. The capsule, which is made from the fabrication of soft polymers, is imprinted with the RPE cells with mCP technique. At this time, surgeons in the ophthalmology department are working on microsurgical techniques for transplanting the newly developed materials into the eye.

Retinal prostheses

For the other 20 percent of AMD-diagnosed patients, all the light-sensitive cells in the retina have died. In these cases, a pinpoint-sized electronic or chemical device capable of receiving light and translating it into nerve-stimulating signals (a retinal prosthesis) would need to be implanted in the eye. Bent's team of researchers is in the process of developing the most physiologically correct prosthesis for the retina. "It's been a learning process so far," says Bent. "The first prototype shown was made out of silicon, a very hard material, but this doesn't conform easily to the curvature of the eye. So now we're trying to use the same general ideas to make it out of polymers. The idea is the polymer material can be rapidly prototyped and will be flexible enough for the ultimate implementation in the retina."

While the group is working on both electrical and chemical chips, the focus in the past has been on the electrical aspect, since the use of nerve-stimulating electrodes has been the more common approach. However, the nerve-stimulating electrodes are cumbersome (in terms of size) when used with the electrical chips. Therefore, Bent has turned her attention toward the chemical chip. "We are dealing with trying to effectively inte-



^ The architecture of RPE cells, which is vital to the functional integrity of the eye, is a layer of tightly packed, hexagonal cells, as seen above. (Courtesy of Richard Hunt.)

grate microfluidic capillaries with apertures that will release the fluid," says Bent in describing the development of the chemical chip. However, the chemical aspect of the device must also incorporate electrical power, though of a different form. The fluid flows through a process known as electro-osmotic flow, which forces the fluid through the apertures and stimulates the neurons on the other side. The power supply for the chemical chip isn't quite as cumbersome as the electrodes, but it still proves to be a problem. While the team is struggling to overcome these challenges, they have succeeded in establishing models for these retinal prostheses that can be used in tested trials.

Where are they now?

Presently, the team has begun trials of tissue transplant and retinal prostheses with animals, though human trials seem to be in the distant future. The fabrication of soft materials and integration of all the different disciplines has been challenging along the way, but Bent looks at the progress optimistically. "There are a relatively small number of groups working on this research because it takes so many different disciplines to contribute," Bent says. "Stanford is among the few groups worldwide working on an electrical chip and the only group developing a chemical chip."

The new technologies that are being developed with this research have opened the doors in the field of medical prostheses. "I think it's a general enough approach that it can lend itself to neuro-prostheses, to be used with any disease or injury where you might want to stimulate neurons," comments Bent. "The other big application of this is a general drug delivery device, not just for neural stimulation." Bent has said that the most fulfilling part of working on this project is applying the skills of materials science to the medical and biological fields. With the collaboration of so many disciplines to create this new technology of retinal implantation and prosthesis, countless possibilities are undoubtedly waiting to be discovered. S

David Trieu is a freshman, currently considering a major in Chemical Engineering with a minor in Economics. Along with his love of science, David enjoys tennis, basketball, jazz, vanilla chai, and lounging around with nothing to do.